III. REMARKS

Claim Status

Claims 17-18 and 22-28, 30-32 and 34 are active in the case. Claims 1-16 and 21 have been cancelled. Claims 19-20, 29 and 33 are withdrawn from consideration as being directed to a non-elected invention. Claim 32 has been amended. Claim 34 is new.

Claim Objections

Claims 17 and 32 are objected to because Claim 32 depends upon itself and claims 17 and 32 are both drawn to the mammal being a human, therefore it appears that the claims may be repetitive.

The typographical error in claim 32 has been corrected thus obviating this ground for objection.

Claim Rejections - 35 USC § 103

Claims 17-18, 22-28 and 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dasseux et al., (WO 99/16458 published April 8, 1999) or Dasseux et al., (USP 6,004,925 published December 21, 1999) in view of Rozek et al., (Biochemistry. 1995. Vol. 34, pages 7401-7408).

Applicant traverses these grounds for rejection.

In order to combine these two references, one of which discloses ApoA1 and the other ApoC1, the examiner has to show the similarities between ApoA1 and ApoC1. The examiner attempts to do this, slowing several similarities between the two apoproteins.

But the similarities stop short of the crucial difference between the two apoproteins.

The working mechanism of apoC1 in sepsis is not through uptake (via an LDL receptor) as is the case with lipid uptake by the liver, but through binding to the toxic LPS of bacteria and the effects of this binding on the response generated via the TOLL-like receptor that mediates the immune response to these toxic components.

Further, although both apoA1 and apoC1 are apolipoproteins, they differ enormously:

1] they do not show a significant homology in their amino acid sequence,

2] apoA1 is 5 times as big as apoC1 and

3] the domains of apoC1 that bind to the LPS are completely different from apoA1.

The molecules differ too much to suggest a similar working mechanism based on structural similarities. It is respectfully suggested the any suggestion of obviousness (which as demonstrated above is absent) could only be based on impermissible hindsight.

The present invention discloses that ApoCl or parts of apoC1 containing a certain sequence KVKEKLK, and two sequences containing that sequence: particularly the sequence MREWFSETFQKVKEKLK, or its truncated version MREWFSETFQKVKEK. As identified in the present claim 27, these sequences bind LPS and consequently can be used to counteract the harmful effects of LPS in the body.

The particular ApoCl sequence involved in LPS binding is unique for ApoC1 and does not occur in ApoAl.

This is not surprising. The overall similarity between ApoCl and ApoA1 is low: mature ApoAl is 243 amino acid residues long whereas ApoCl is only 57 amino acids long.

What is surprising is the other members of the ApoC family, much closer to each than they are to apoA1 do not have the same functionalities.

At paragraph [0031] of applicants published application applicant distinguishes apoC1 from apoCIII. This is reiterated at paragraph [0084].

The fact apo proteins of the same family do not have the same functionality would lead one skilled in the away from trying an apolipoprotein of different family. Consequently, as the apoA and apoC molecules belong to different apolipoprotein families it does not follow that the functionalities of one are present in the other. The only clear similarity of the two molecules is the presence of helical lipid binding structures in both molecules as mentioned before, completely in line with the lipid binding properties of all apolipoproteins.

Rozek et al. do not disclose the fragments that applicants are claiming. Rozek et al. specifically identify apoCl1 (1-38) and apoC1 (35-53), wherein they have identified amphipathic helical regions spanning residues V4-K30 and R39-E51 (see page 1866, left column). Although two of the identified regions (35-53 and 39-51) overlap with the sequences as

provided in the present application, the exactly claimed stretches of amino acids have not been disclosed by Rozek at al.

A person skilled in the art would by reading the two cited works by no means become inclined to combine these and propose to use ApoC1 to bind harmful LPS in order to counteract sepsis.

Also as stated by the examiner, Dasseux et al. also each the peptide design is based on the helical structure and amphipathic properties of a 22 amino acid consensus sequence derived from the helical repeats of ApoA1; and that the agonist can be used to treat any animals, especially mammals, including humans for enotoxemia which results in septic shock.

Dasseux et al. disclose a relation is shown between structural aspects of ApoA1 and their application for treating dyslipidemic disorders. A crucial component in that disclosure is an ApoAl agonist compound forming an amphipathic helix and the use of such a compound in a pharmaceutical composition.

Rozek et al. disclose that ApoC1 contains similar amphipathic helical structures. The Examiner infers from this information that one skilled in the art by combining these two works would come to the conclusion that the properties and functions of ApoAl and ApoC1, including the effects of the latter in sepsis, are similar.

Applicant believes this conclusion would not be drawn by the one skilled in the art since the observation of some partial similarity in structure between ApoAl and ApoC1 is not remarkable since both Apo proteins (and actually several others)

have in common that they all bind to lipids (their natural function) and that the helical structures have been shown to be involved in lipid binding. The fact that two apoproteins have some structural similarity (having both helical structures) is to be expected based on their natural function,

Favorable reconsideration is respectfully requested.

The Commissioner is hereby authorized to charge payment for any fees associated with this communication or credit any over payment to Deposit Account No. 14-1263.

Respectfully submitted,

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